

Notice of Allowability

Application No.	Applicant(s)
10/006,009	VAN GEMEN ET AL.
Examiner	Art Unit
Diana B. Johannsen	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. This communication is responsive to the After Final amendment of 9/13/04; the interviews of 10/26/04 and 10/27/04.
2. The allowed claim(s) is/are 17-25 and 47-52.
3. The drawings filed on 30 September 2003 are accepted by the Examiner.
4. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some* c) None of the:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
(a) including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 1) hereto or 2) to Paper No./Mail Date _____.
(b) including changes required by the attached Examiner's Amendment / Comment or in the Office action of
 Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. Notice of References Cited (PTO-892)
2. Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. Information Disclosure Statements (PTO-1449 or PTO/SB/08),
 Paper No./Mail Date _____
4. Examiner's Comment Regarding Requirement for Deposit
 of Biological Material
5. Notice of Informal Patent Application (PTO-152)
6. Interview Summary (PTO-413),
 Paper No./Mail Date 1004 (2).
7. Examiner's Amendment/Comment
8. Examiner's Statement of Reasons for Allowance
9. Other _____.

EXAMINER'S AMENDMENT

1. This action is responsive to the After Final Amendment filed September 13, 2004, and the Interviews of October 26, 2004 and October 27, 2004. The After Final Amendment has been entered, and claims 17-25 and 47-52 are now allowed, subject to the Examiner's amendment set forth below.
2. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment that places this application in condition for allowance. During a telephone conversation conducted on October 27, 2004, Andrew F. Nilles requested an extension of time for 2 additional MONTH(S) (for a total of 3 MONTHS) and authorized the Director to charge Deposit Account No. 20-1469 the required fee of \$870 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
3. In accordance with 37 C.F.R. 1.126, allowed claims 17-25 and 47-52 will be renumbered as claims 1-15, respectively (see MPEP 608.01(j)). It is noted that original claim numbers are employed in the below Examiner's amendment.

4. **Amend the claims as follows:**

Amend claim 17 as follows:

17. A method of determining whether a medicament has therapeutic activity and/or possible side-effects, said method comprising:
introducing a medicament to an organism;
determining in a sample obtained from said organism a relative ratio of a first mitochondrial nucleic acid and/or gene product thereof ~~of an endosymbiotic cellular organelle to any second to a chromosomal~~ nucleic acid and/or gene product thereof of ~~said organism in a sample obtained from said organism~~; and
determining whether there is a change in the relative ratio ~~before, during and/or after introduction of the medicament, wherein said change in said relative ratio is indicative of a therapeutic activity and/or a side effect of the medicament that said medicament has therapeutic activity and/or possible side-effects.~~

In claim 47, line 2, delete "first" and insert therefore—mitochondrial--.

In claim 47, line 2, delete "second" and insert therefore—chromosomal--.

In claim 47, line 3, delete "with said sample".

In claim 48, line 2, delete "first" and insert therefore—mitochondrial--.

In claim 48, line 2, delete "second" and insert therefore—chromosomal--.

In claim 48, line 3, delete "with said sample".

In claim 49, line 2, delete "first" and insert therefore—mitochondrial--.

In claim 49, line 3, delete "second" and insert therefore—chromosomal--.

In claim 50, line 2, delete "second" and insert therefore—chromosomal--.

In claim 50, line 3, delete "first" and insert therefore—mitochondrial--.

In claim 52, line 1, delete "first" and insert therefore—mitochondrial--.

In claim 52, line 2, delete "second" and insert therefore—chromosomal--.

5. It is noted that the examiner has changed the title of the application to:

Method of determining therapeutic activity and/or possible side-effects of a medicament.

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5. The following is an examiner's statement of reasons for allowance.

It is noted that while the prior art as exemplified, e.g., by de Muys et al (Antimicrobial Agents and Chemotherapy 43(8):1835-1844 [8/1999]) teaches that ratios of mitochondrial to nuclear DNA may serve as indicators of toxicity in cultured cells (see, e.g., page 1841 of de Muys et al), the prior art as exemplified by, e.g., Brinkman et al (Current Opinion in Infectious Diseases 13(1):5-11 [2/2000]; see particularly page 6) and Moyle (Clinical Therapeutics 22(8):911-936 [8/2000]; see particularly page 913) indicates that such *in vitro* findings are not correlative with toxicity *in vivo*. Thus, the prior art does not teach or suggest that such ratios may be employed successfully in determining therapeutic activity and mitochondrial toxicity in organisms (e.g., in patient populations), as exemplified by Applicants (see, e.g., Example 20).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Diana B. Johannsen
Primary Examiner
October 28, 2004